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Substitu	te for form 1449/PTO			Application Number	10/813,177		
INF	ORMATION	N DIS	CLOSURE	Filing Date	03/29/04		
STA	TEMENT	BY A	PPLICANT	First Named Inventor	Wei Gu		
	***			Art Unit	1646		
	(Use as many sh	eets as r	iecessary)	Examiner Name	to be assigned		
Sheet	1	of	16	Attorney Docket Number	5199-178		

		NON PATENT LITERATURE DOCUMENTS	
Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
/B.F./ Appella and Anderson, Signaling to p53: breaking the posttranslational modification code.			
/B.F./		Pathol. Biol. (Paris), 48:227-45, 2000	
/B.F	/	Ashcroft et al., Regulation of p53 function and stability by phosphorylation.	
		Mol. Cell Biol., 19:1751-58, 1999	
		Ashcroft et al., Stress signals utilize multiple pathways to stabilize p53.	
		Mol. Cell Biol., 20:3224-33, 2000	
		Ashcroft and Vousden, Regulation of p53 stability.	
		Oncogene, 18:7637-43, 1999	
$\overline{\downarrow}$		Barak et al., mdm2 expression is induced by wild type p53 activity.	
/B.F./	,	EMBO J., 12:461-68, 1993	

Orginator Company of the Company of	Examiner Signature	/Brandon Fetterolf/	Date 10/12/2007 Considered
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/B.F./		Beers and Berkow (eds.), The Merck Manual of Diagnosis and Therapy, 17th ed. (Whitehouse Station, NJ: Merck Research Laboratories, 1999)			
		973-74, 976, 986, 988, 991 (N/A)			
		Blattner et al., DNA damage induced p53 stabilization: no indication for an involvement of p53 phosphorylation.			
		Oncogene, 18:1723-32, 1999			
		Bodansky, M., Principles of Peptide Synthesis (New York: Springer-Verlag New York, Inc., 1984			
		Botchkarev et al., p53 is essential for chemotherapy-induced hair loss.			
$\overline{\mathbf{V}}$		Cancer Res., 60:5002-02, 2000			
ים בי		Brooks and Gu, Ubiquitination, phosphorylation and acetylation: the molecular basis for p53 regulation.			
/B.F./		Curr. Opin. Cell Biol., 15:164-71, 2003 (N/A)			
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Signature	/Brandon Fetterolf/	Considered	10/12/2007

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INF	ORMATIO	N DIS	CLOSURE	Filing Date	03/29/04	
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/B.F	./	Chen et al. (Mapping of the p53 and mdm-2 interaction domains.	
		Mol. Cell. Biol., 13:4107-14, 1993	
		Chung and Baek, Deubiquitinating enzymes: their diversity and emerging roles.	
		Biochem. Biophys. Res. Commun., 266: 633-640, 1999	
		D'Andrea and Pellman, Deubiquitinating enzymes: a new class of biological regulators.	
		Crit. Rev. Biochem. Mol. Biol., 33:337-52, 1998	
		de Graaf et al., Hdmx protein stability is regulated by the ubiquitin ligase activity of Mdm2.	
		J. Biol. Chem., 278:38315-324, 2003	
		Donehower et al., Mice Deficient for p53 are developmentally normal but susceptible to spontaneous tumours.	
/B.F./		Nature, 356:215-21, 1992	

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Signat	ture /Brandon Fetterolf/	Considered	

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	Dumaz and Meek, Serine15 phosphorylation stimulates p53 transactivation but does not directly influence interaction with HDM2.				
	EMBO J., 18:7002-10, 1999				
	el-Deiry et al., WAF1, a potential mediator of p53 tumor suppression.				
	Cell, 75:817-825, 1993				
	Everett et al., A novel ubiquitin-specific protease is dynamically associated with the PML nuclear domain and binds to a herpesvirus regulatory protein.				
	EMBO J., 16:566-77, 1997				
	Finch et al., Mdmx is a negative regulator of p53 activity in vivo.				
	Cancer Res., 62:3221-225, 2002				
	Freedman et al., Functions of the MDM2 oncoprotein.				
./	Cell Mol. Life Sci., 55:96-107, 1999				
		No.¹ the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published. Dumaz and Meek, Serine15 phosphorylation stimulates p53 transactivation but does not directly influence interaction with HDM2. EMBO J., 18:7002-10, 1999 el-Deiry et al., WAF1, a potential mediator of p53 tumor suppression. Cell, 75:817-825, 1993 Everett et al., A novel ubiquitin-specific protease is dynamically associated with the PML nuclear domain and binds to a herpesvirus regulatory protein. EMBO J., 16:566-77, 1997 Finch et al., Mdmx is a negative regulator of p53 activity in vivo. Cancer Res., 62:3221-225, 2002 Freedman et al., Functions of the MDM2 oncoprotein.			

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Signature	/Brandon r daoron/	Considered	10/12/2007

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INF	ORMATION	DIS	CLOSURE	Filing Date	03/29/04	
STA	STATEMENT BY APPLICANT			First Named Inventor	Wei Gu	
				Art Unit	1646	
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Sheet	5	of	16	Attorney Docket Number	5199-178	

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/B.F	./	Giaccia and Kastan, The complexity of p53 modulation: emerging patterns from divergent signals.			
		Genes Dev., 12:2973-83, 1998			
		Gu et al., Mutual dependence of MDM2 and MDMX in their functional inactivation of p53.			
		J. Biol. Chem., 277:19251-254, 2002			
		Gu et al., Synergistic activation of transcription by CBP and p53.			
		Nature, 387:819-23, 1997			
		Haupt et al., Mdm2 promotes the rapid degradation of p53.			
		Nature, 387:296-99, 1997			
\bigvee		Hemann et al., An epi-allelic series of p53 hypomorphs created by stable RNAi produces distinct tumor phenotypes in vivo.			
/B.F	./	Nat. Genet., 33:396-400, 2003 (N/A)			

Examiner Signature	/Brandon Fetterolf/	Date Considered	10/12/2007

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/B.F./		Hengstermann et al., Complete switch from Mdm2 to human papillomavirus E6-mediated degradation of p53 in cervical cancer cells.	
		Proc. Natl. Acad. Sci. USA, 98:1218-23, 2001	
		Hershko et al., The ubiquitin system.	
		Nat. Med., 6:1073-81, 2000	
		Hicke and Dunn, Regulation of membrane protein transport by ubiquitin and ubiquitin-binding proteins.	
		Annu. Rev. Cell Dev. Biol., 19:141-72, 2003	
		Hollstein et al., Database of p53 gene somatic mutations in human tumors and cell lines.	
		Nucleic Acids Res., 22:3551-55, 1994	
$\overline{\mathbf{V}}$		Hollstein et al., New approaches to understanding p53 gene tumor mutation spectra.	
/B.F./		Mutat. Res., 431:199-209, 1999	

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/B.F./		Holowaty et al., Protein interaction domains of the ubiquitin-specific protease, USP7/HAUSP.	
		J. Biol. Chem., 278: 47753-47761, 2003	
		Holowaty et al., Protein profiling with Epstein-Barr nuclear antigen-1 reveals an interaction with the herpesvirus-associated ubiquitin-specific	
		protease HAUSP/USP7.	
		J. Biol. Chem., 278:29987-994, 2003	
		Honda et al., Oncoprotein MDM2 is a ubiquitin ligase E3 for tumor suppressor p53.	
		FEBS Lett., 420:25-27, 1997	
$\sqrt{}$		Jones et al., Rescue of embryonic lethality in Mdm2-deficient mice by absence of p53.	
/B.F./		Nature, 378:206-08, 1995	

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Sheet 8 Art Unit 1646 **Examiner Name** to be assigned Attorney Docket Number 5199-178

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/B.F.	'	Kamijo et al., Tumor suppression at the mouse INK4a locus mediated by the alternative reading frame product p19ARF.	
		Cell, 91:649-59, 1997	
		Kastan et al., A mammalian cell cycle checkpoint pathway utilizing p53 and GADD45 is defective in ataxia-telangiectasia.	
		Cell, 71:587-97, 1992	
		Kawai et al., DNA damage-induced MDMX degradation is mediated by MDM2.	
		J. Biol. Chem., 278:45946-953, 2003	
		Kornitzer and Ciechanover, Modes of regulation of ubiquitin-mediated protein degradation.	
		J. Cell. Phys., 182:1-11, 2000	
		Kubbutat et al., Regulation of p53 stability by Mdm2.	
/B.F./		Nature, 387:299-303, 1997	

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/B.F./		Lane, D.P., p53, guardian of the genome.						
		Nature, 358:15-16, 1992						
		Laney and Hochstrasser, Substrate targeting in the ubiquitin system.						
		Cell, 97:427-30, 1999						
		Levine, A.J., p53, the cellular gatekeeper for growth and division.						
		Cell, 88:323-31, 1997						
		Linares et al., HdmX stimulates Hdm2-mediated ubiquitination and degradation of p53.						
		Proc. Natl. Acad. Sci. USA, 100:12009-014, 2003						
		Luo et al., Deacetylation of p53 modulates its effect on cell growth and apoptosis.						
/B.F./		Nature, 408:377-81, 2000						

		
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/B.F./		Luo et al., Negative control of p53 by Sir2• promotes cell survival under stress.				
		Cell, 107:137-48, 2001				
	-	Lowe and Sherr, Tumor suppression by Ink4a-Arf: progress and puzzles.				
		Curr. Opin. Genet. Dev., 13:77-83, 2003 (M/A)				
		Michael and Oren, The p53-Mdm2 module and the ubiquitin system.				
		Semin. Cancer Biol., 13:49-58, 2003				
		Migliorini et al., Mdm4 (Mdmx) regulates p53-induced growth arrest and neuronal cell death during early embryonic mouse development.				
V		Mol. Cell Biol., 22:5527-38, 2002				
/B.F./		Modern Techniques of Peptide and Amino Acid Analysis (New York: John Wiley & Sons, 1981				

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/B.F./		Montes de Oca Luna et al., Rescue of early embryonic lethality in mdm2-deficient mice by deletion of p53.	
		Nature, 378:203-06, 1995	
		Munger and Howley, Human papillomavirus immortalization and transformation functions.	
		Virus Res., 89:213-28, 2002	
		Nakano and Vousden, PUMA, a novel proapoptotic gene, is induced by p53.	
		Molecular Cell, 7:683-94, 2001	
		Oda et al., Noxa, a BH3-only member of the Bcl-2 family and candidate mediator of p53-induced apoptosis.	
		Science, 288:1053-58, 2000a	
$\sqrt{}$		Oda et al., p53AlP1, a potential mediator of p53-dependent apoptosis, and its regulation by Ser-46-phosphorylated p53.	
/B.F./		Cell, 102:849-62, 2000b	

Examiner	/Brandon Fetterolf/	Date Considered	10/12/2007
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Sheet	12	of	16	Attorney Docket Number	5199-178	

Examiner Initials*	Cite No. ¹				
/B.F./		Okamoto and Beach, Cyclin G is a transcriptional target of the p53 tumor suppressor protein.			
		EMBO J., 13:4816-22, 1994			
		Oren, M., Regulation of the p53 tumor suppressor protein.			
		J. Biol. Chem., 274, 36031-034, 1999			
		Pan and Chen, MDM2 promotes ubiquitination and degradation of MDMX.			
		Mol. Cell Biol., 23:5113-21, 2003			
		Parant et al., Rescue of embryonic lethality in Mdm4-null mice by loss of Trp53 suggests a non-overlapping pathway with MDM2 to regulate p53.			
		Nat. Genet., 29:92-95, 2001			
		Pickart, C.M., Back to the future with ubiquitin.			
/B.F./		Cell, 116:181-90, 2004			

Examiner	/Dunindan Fattonals/	Date	10/12/2007
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/B.F./		Prives and Hall, The p53 pathway.	
		J. Pathol., 187:112-26, 1999	
		Rodriguez et al., Multiple C-terminal lysine residues target p53 for ubiquitin-proteasome-mediated degradation.	
		Mol. Cell. Biol., 20:8458-67, 2000	
	-	Scheffner et al., The HPV-16 E6 and E6-AP complex functions as an ubiquitin-protein ligase in the ubiquitination of p53.	
		Cell, 75:495-505, 1993	
		Seavey et al., The E7 oncoprotein of human papillomavirus type 16 stabilizes p53 through a mechanism independent of p19 (ARF).	
		J. Virol., 73:7590-98, 1999	
		Sherr, C.J., The INK4a/ARF network in tumour suppression.	
/B.F./		Nat. Rev. Mol. Cell Biol., 2:731-37, 2001	

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/B.F./		Sherr and Webber, The ARF/p53 pathway.	
		Curr. Opin. Genet. Dev., 10:94-99, 2000	
		Shieh et al., DNA damage-induced phosphorylation of p53 alleviates inhibition MDM2.	
		Cell, 91:325-34, 1997	
		Slingerland and Pagano, Regulation of the cdk inhibitor p27 and its deregulation in cancer.	
		J. Cell Physi., 183:10-17, 2000	
		Stad et al., Mdmx stabilizes p53 and Mdm2 via two distinct mechanisms.	
		EMBO Rep., 2:1029-34, 2001	
		Stott et al., The alternative product from the human CDKN2A locus, p14(ARF), participates in a regulatory feedback loop with p53 and MDM2.	
/B.F./		EMBO J., 17:5001-14, 1998	

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			Tolbert et al., p19ARF is dispensable for oncogenic stress-induced p53-mediated apoptosis and tumor suppression in vivo.	
			Mol. Cell Biol., 22:370-77, 2002	
		•	Tyner et al., p53 mutant mice that display early ageing-associated phenotypes.	
			Nature, 415:45-53, 2002 (N/A)	
			Vogelstein et al., Surfing the p53 network.	
			Nature, 408:307-10, 2000	
			Wilkinson, K.D., Signal transduction: aspirin, ubiquitin and cancer.	
			Nature, 424:738-39, 2003	
	,		Wilkinson, K.D., Ubiquitination and deubiquitination: targeting of proteins for degradation by the proteasome.	
/B.	.F./		Semin. Cell Dev. Biol., 11:141-48, 2000	

Examiner		Date	10/12/2007
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/B.F./		Wu et al., The p53-mdm-2 autoregulatory feedback loop.	
		Genes Dev., 7:1126-32, 1993	
V		Yu et al., PUMA induces the rapid apoptosis of colorectal cancer cells.	
/B.F./		Molecular Cell, 7:673-82, 2001	
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